UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/247,874	02/10/1999	GORDON W. DUFF	MSA-004.01	8151

30623 7590 09/09/2004

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/247,874	DUFF ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,46-64 and 70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *34,46-64 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 6/10/04. New claim 70 was added.

Claims 34, 46-64 and 70 are pending and under consideration in this Office Action.

Previously it was indicated that claim 34 was allowable. After further consideration, and careful consideration of the specification as filed and the Declaration of Dr. di Giovine filed 3/2/01, this finding is withdrawn. See below for a detailed discussion.

Prosecution History

The specification as filed indicated that Applicant had discovered a novel allele of IL1-beta comprising a G residue at position +6912, whereas the prior art disclosed a C residue at this position. The specification disclosed SEQ ID NOS: 1 and 2, and Figures 1 and 2, each of which was 9721 nucleotides in length. However, these sequences as originally filed all disclosed a G at +6912 (position 8845 of the SEQ ID NOS), and the specification as filed did not disclose any 9721 nucleotide sequence with a C at position +6912. A search of the prior art revealed that position +6912 of IL-1B was known to be a G and not a C residue, and claims were rejected under 35 USC 102 over the prior art (Clark et al) in the Office Action of 3/29/2000. Applicant subsequently amended the specification and Sequence Listing, and indicated that the identification of the novel allele as having a G residue at position +6912 was an inadvertent error, and that the invention comprised a C residue at position +6912, whereas the prior art allele

comprised a G at this position. The next Office Action indicated that this amendment introduced new matter into the disclosure, and that in order to overcome the new matter rejection, Applicant needed to establish that, at the time of filing, they were in possession of the claimed invention, i.e. a polynucleotide identical to that disclosed in Figure 1 , except that it comprises a C rather than a G at position 6912. Furthermore Applicant needed to establish that the IL-IB sequence comprising a G residue at position 6912 (human IL-IB GEN XO4500) was recognized in the prior art as the wild type sequence, and that the nucleic acid of the instant invention was, in fact, not wild type. In response Applicant submitted the declaration of Dr. di Giovine on 3/2/01, that indicated that the prior art taught a G at position +6912, that a C at this position had been discovered by Applicant, and that Applicant had named the prior art allele comprising G at 6912 as "allele 1" and the allele comprising C at 6912 as "allele 2". The declaration was supported by output from an automated nucleic acid sequencer showing approximately 340 bases of sequence, including a C at position 199, which appeared to correspond to position +6912 of the IL-1B sequence. Declarant also indicated that the specification taught that allele 1 was the more frequently occurring allele in nature, and so it could be considered the wild type allele. Based on this declaration, the new matter rejection was withdrawn. After further consideration, it is found that the rejection was withdrawn in error, and that amendments to the specification, figures, and Sequence Listing that indicate that position +6912 of alleles 1 and 2 are G and C residues, respectively, introduce new matter into the disclosure as discussed more fully below.

Specification

The amendment filed 7/3/2000 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment to page 4, line 27 changing guanine to cytosine is new matter.

The amendments to page 6 lines 32 and 33, page 10, line 11, page 37, line 8, and page 38, line 8, requiring substitution of cytosine (c) for guanine (G) and vice versa, are new matter.

The amendment at page 38, line 11 replacing "2" with --1-- is new matter.

Figure 2D filed 2/8/2002 comprises new matter in that it comprises a C residue at position 6912.

The Sequence Listing submitted 1/26/04 comprises new matter in that it comprises as C residue at position 8845 of SEQ ID NO:2.

In support of the preceding amendments, Applicant argued that the indication in the specification as filed that alleles 1 and 2 comprised C and G residues, respectively, at position 6912 was an inadvertent error, and that alleles 1 and 2 actually comprised a G and C residues respectively at position 6912. This argument was subsequently supported by the declaration of Dr. di Giovine on 3/2/2001. The declaration indicated that the prior art taught a G at position 6912, that a C had been discovered by Applicant, and that Applicant had named the prior art allele comprising G at 6912 as "allele 1" and

the allele comprising C at 6912 as "allele 2". The declaration was supported by output from an automated nucleic acid sequencer showing approximately 340 bases of sequence, including a C at position 199, which appeared to correspond to position 6912 of the IL-1 beta sequence. Declarant also indicated that the specification taught that allele 1 was the more frequently occurring allele in nature, and so it could be considered the wild type allele.

In response the PTO notes the following. There is no doubt that Applicant has discovered that there is a polymorphism at position +6912 of the IL-1B gene. There is no doubt that the previously published sequence had a guanine at +6912 and that Applicant amplified a portion of an IL-1B gene and discovered a cytosine at +6912. However, Applicant's arguments and the declaration do not provide sufficient evidence to show that Applicant was in possession of amended SEQ ID NO:2, and the sequence set forth in amended Fig. 2, at the time of filing. These sequences are 9721 bases in length, and differ from the prior art IL-1B sequence (GEN XO4500) only at position +6912, which has been converted to C from G. However, neither the specification nor declaration as filed supports a 9721 nucleotide sequence of IL-1B with a C at the +6912 polymorphic site. The originally filed SEQ ID NOS: 1 and 2 and Figures 1 and 2 all disclosed a G at +6912. The specification at page 36 shows that the polymorphism was detected on a 403 base PCR fragment of the IL-1B gene, and the declaration of 3/2/01, shows about 340 bases of sequence comprising the polymorphism. This does not provide support for the 9721 bases of sequence in amended SEQ ID NO:2 and Fig. 2 that have a C residue at the polymorphic position. Since polymorphisms can occur

throughout a molecule, one cannot assume that there are no other polymorphisms linked to position +6912 within the 9721 bases of the IL-1B gene, and that the sequence of the rest of the 9721 nucleotides is identical to that reported in the prior art. As such, absent supporting evidence, one cannot simply assume that the Applicant was in possession of amended SEQ ID NO:2, or Fig. 2, at the time of filing. The declaration fails to provide such evidence.

In addition, the changes to the specification which reverse the designations of "allele 1" and "allele 2" appear to represent new matter. Applicants state in the arguments "the sequencing revealed a novel G to C mutation that is referred to herein as the IL-1B(+6912) allele 2." There is no disclosure in the specification to indicate that this is the case. The specification as filed does not refer to the "C" allele of this polymorphism as allele 2, instead it very clearly defines the "C" allele of this polymorphism as allele 1 (See specification page 6, line 31 and specification page 38 line 11 which exemplifies a probe to allele 2). It is established that "An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction (MPEP 2167.03(II))." Thus, one must determine whether or not the correction of the specification herein is an obvious error.

Applicants assert in the di Giovine declaration that the "cytosine" allele of the disclosed polymorphism was referred to in the laboratory as "allele 2" of the two possible polymorphic alleles (declaration ¶ 6). However, this is not supported by the specification. The specification very clearly identifies allele 1 as being the cytosine

allele and allele 2 as being the guanine allele on page 6, line 31, and is consistent with this definition throughout. The examples teach the amplification of a 403 bp fragment of the 3'UTR of the IL-1B gene and sequencing of the gene and discovery of a novel C to G polymorphism (Example 1, beginning on p. 37).

Applicants teach in example 2 that the IL-1B allele 2 was found in a population of 820 individuals at a frequency of 0.266. In the declaration, applicants state that "allele 1 is the more frequent allele and may therefore be considered the wild-type allele." In this example applicants teach a probe for allele 1 (SEQ ID NO: 8) which has a "C" at the polymorphic position, and a probe for allele 2 (SEQ ID NO: 9) which has a "G" at the polymorphic position. The remainder of the examples refer only to the alleles by their numerical identifiers.

A possible explanation for the disclosure in the specification which is consistent with the data and examples presented in the specification is as follows:

(a) There is a known version of the IL-1B gene which has a G at position +6912.

(b) Applicants sequenced a PCR fragment of the 3' UTR containing this position.

(c) Applicants discovered a C at this position in the PCR fragment.

(d) Applicants screened a population of 820 people and discovered that the "C" allele is more frequent. Applicants assigned the arbitrary designator "allele 1" to the "C" allele. Applicants assigned the arbitrary designator "allele 2" to the "G" allele.

Applicants have provided another possible explanation of the specification which is contingent upon a recognition that there was an error to begin with. It is not clear from the specification as filed that applicant even erred in their reference to the

particular alleles. In fact, the specification as filed appears to be totally consistent with itself in reference to allele 1 and allele 2 as being a "C" for allele 1 and a "G" for allele 2. Thus, it does not seem that the error would have been recognized on its face by a reading of the specification by one skilled in the art, and more to the point, even if the error were clear, the solution to the problem is not readily apparent from a reading of the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 54-57 are objected to objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 54-57 are drawn to the isolated nucleic acid of claim 46 further comprising a label, or bound to a solid phase support. However, claim 46 is drawn to an isolated nucleic acid **consisting of** a nucleic acid sequence. The claim uses closed language to describe the nucleic acid. As a result, claims 54-57 do not further limit the isolated nucleic acid set forth in claim 46, instead, they improperly add matter which is not accounted for in claim 46, i.e. a label or a solid support. Because they do not further limit claim 46, but instead broaden it, claims 54-57 are improper dependent claims.

Claim 70 is objected to because "nuleic" is misspelled. Claim 70 is also objected to because of the relationship implied by the phrase "second nucleic acid comprises a

vector" is inverted for many embodiments. The term "vector" embraces a broad scope of compositions including e.g. plasmids, viruses, liposomes, polycationic polymers, microspheres, and other particulate compositions. In the context of a plasmid vector, it is reasonable to say that a nucleic acid may comprise a vector, particularly in the form of a "vector backbone." However, in situations where the vector is a virus or other particulate carrier associated with a nucleic acid, the vector comprises elements that are not nucleic acid in nature, i.e. proteins, or lipids, or polycations, or particles, that while associated with the nucleic acid, are not "comprised" by it. Instead it is more conventional to say that the vector comprises the nucleic acid because the vector generally encapsulates or otherwise mediates delivery of the nucleic acid. IN order to clarify the claim. it is suggested that the word "is" should be substituted for the word "comprises".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 34, 46-64 and 70 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to SEQ ID NO:2, or to fragments thereof comprising position 8845 (which is the same as IL-1B position +6912 discussed above). As discussed at length above, one of skill in the art could not have come to the conclusion that Applicant was in possession of SEQ ID NO:2 (as amended) at the time the invention was filed. SEQ ID NO:2 as amended is 9721 bases in length and contains a C residue at position 8845 that has been identified as a polymorphic position. However, the specification as filed did not disclose a 9721 nucleotide sequence with a C at position 8845, and the addition of such a sequence to the disclosure represents new matter such that one of skill in the art could not come to the conclusion that Applicant was in possession of SEQ ID NO:2 at the time of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 53 is rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796, issued 12/12/95).

Brennan teaches an array of isolated oligonucleotides comprising every conceivable 10mer oligonucleotide sequence. See column 9, lines 48-55. Thus Brennan teaches every 10 nucleotide complement of SEQ ID NO: 2. this rejection can be overcome by amending claim 53 to require complementarity to the entire length of the nucleic acid of claim 46.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

DAVE T. NGUYEN
PRIMARY EXAMINER

Richard Schnizer, Ph.D.